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On the Use of MPC Techniques to Decide Intervention Policies against COVID-19

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Abstract:

This paper aims at demonstrating how and that model predictive control (MPC) strategies can be used to determine optimal intervention policies against the COVID-19 pandemic. Especially for the time after a first wave of infection and before a vaccine can be safely distributed to a sufficient extent, the intervention experience from the first outbreak can be utilized to guide the policy decision in this period. The MPC problem in this paper takes the pandemic in different regions of a country and its neighboring countries into account, while policies such as wearing masks or social distancing are selected as inputs to be optimized. This optimized policy balances the risk of a second outbreak and socio-economic costs, while considering that the measure should not be too severe to be rejected by the population. Effectiveness of this policy compared to standard intervention policies is compared through numerical simulations.

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1. INTRODUCTION

The outbreak of COVID-19 in 2020 has changed the life of virtually almost everyone on the planet. The rapid spread of the virus, together with the high mortality rate in the early period of the outbreak, forced the governments to deploy intervention policies such as lock-down of cities, or restricting the social life considerably. These policies have indeed shown their effect on controlling the spread of the virus, but also caused significant harm to the economies. In addition, parts of the populations of many countries have become annoyed by restrictions, and the desire for returning to normal has been getting stronger with time. However, recent observations revealed that second (or later) waves of infection can indeed be triggered once the policies are relaxed, and these waves are experienced to have higher amplitudes than the first one in several countries. As the availability and distribution of vaccines still is a certain time ahead (as of November 2020), governments are forced to deploy restrictions like lock-down policies again in order to mitigate the second or a later wave. Simple intervention scheme of the type of bang-bang control, as switching repeatedly between complete shutdown and no restrictions, quickly lets authorities loose credibility, and the effectiveness of intervention measures gradually decreases over time. This raises the question of which intervention schemes are more suitable, and this paper intends to address this question from the perspective of control theory.

This paper aims at illustrating and investigating the use of model-predictive control (MPC) to determine intervention schemes against COVID-19 which are continuously adapted to the evolution of the pandemic and optimized with respect to a chosen criterion. The goal is to use the experience gathered during the first wave of infection, such

as the average infecting rate of the virus, the average healing time of the patients, effectiveness of different policies in controlling the spread of the virus, or the socio-economic costs of these policies. The intervention policies considered here include, among others, wearing masks, social distancing in different regions, reserving medical staff for COVID-19 patients, or introducing traffic limitation between different regions and countries. The geographic adjacency between regions is also taken into account, such that each region can deploy its own policy against the virus. This setting can help to evaluate whether a common intervention policy of different regions is necessary. It is stressed here that, while the models and measures are adapted to the COVID-19 pandemic, the insights and findings should be transferable with suitable modifications to other pandemics as well. The next section first provides a review on existing work on epidemic modeling and control problems. with distinction of whether the work refers to periods before or after the outbreak of COVID-19. In Sec. 3, the nonlinear epidemic model, the input and state constraints, and the cost functions of the considered MPC approach are specified. Section 4 compares strategies obtained from MPC with simpler schemes such as bang-bang policies. To address the uncertainties of modeling the spread of the virus and thus the influence to the corresponding MPC problems, different extensions are introduced in Sec. 5, before Sec. 6 concludes the paper.

2. LITERATURE REVIEW

To model the spread of a virus, the susceptible - infected - susceptible (SIS) model has been developed in Kermack and McKendrick (1932); Wang et al. (2003): Any individual is either infected, or susceptible to infection at any time in this model, and it is assumed that a susceptible

person may be infected by neighboring persons with some given infection rate, where the network graph structure determines the connectivity between persons. An infected person may be cured with certain healing rate, and by this returns to the state of being susceptible. Based on the SIS model, a 2^n continuous-time Markov model has been introduced in Van Mieghem et al. (2008), where the number 2 denotes the two states of a person, susceptible or infected, and n denotes the total number of people in the graph. The healing and infection of any person $i \in N = \{1, \dots, n\}$ of a Markov model are described by two independent Poisson processes with rates δ_i and β_i , respectively. Although the 2^n Markov model describes the spread of a virus disease often fairly well, its shortcoming is obvious: the state-space size grows exponentially with the number n. Accordingly, an N-Intertwined model has been proposed in Gourdin et al. (2011), in which a mean-field type approximation technique is applied to approximate the 2^n Markov model. This approximation enables one to only use a set of nnonlinear ordinary differential equations to describe the dynamics of the epidemic, i.e., by using $p_i(t)$ to denote the probability of person i being infected in time t, the following dynamics applies:

$$\dot{p}_i(t) = (1 - p_i(t))\beta_i \sum_{j \in N} \alpha_{ij} p_j(t) - \delta_i p_i(t), \quad i \in N. \quad (1)$$

In addition to δ_i and β_i representing the local healing and infection rate of person i, the α_{ij} in (1) corresponds to the connectivity between two persons i and j in a connection graph (while each node of the graph represents a person). In general, an adjacency matrix A can be introduced to describe the connection graph among the people, where α_{ij} denotes an entry of matrix A, and $\alpha_{ij} = 1$ applies if i and j are connected, while $\alpha_{ij} = 0$ otherwise, and $\alpha_{ii} = 1$ for all $i \in N$. Note that if the index i refers to a group of persons instead of an individual (which is the case in the rest of this paper), then the $p_i(t)$ in (1) represents the percentage of infection of a group with index i. The dynamics (1) can also be written in matrix form:

$$\dot{p}(t) = (BA - D)p(t) - diag(p_i(t))BAp(t),$$
 (2)
where $p(t) = [p_1(t), \dots, p_n(t)]^T$, $B = diag(\beta_i)$ and $D = diag(\delta_i)$. As the extinction of the disease implies $p(t) = 0$ in (2), research has focused on determining stability conditions for the origin of (2). First of all, one of the most important indices in epidemiology, the basic reproduction number $R_0 = \rho(D^{-1}A^TB)$, is derived from this model, where ρ denotes the spectral radius of a matrix, see Khanafer et al. (2016). It has been proven that if $R_0 \leq 1$, then the disease-free equilibrium (DFE) is asymptotically stable. In case $R_0 > 1$, there also exists a unique endemic equilibrium which is asymptotically stable according to Fall et al. (2007). This endemic equilibrium also refers to herd immunity.

The research is then extended to account for homogeneous or heterogeneous cases, i.e., whether the healing and infection rate are identical or different for all people. Given the epidemic model (2), the following optimal control tasks have been proposed in literature: 1.) An optimal vaccine allocation plan is considered in Wan et al. (2007); Preciado et al. (2013) and the task there is to investigate how to effectively distribute the vaccine; 2.) The work in Sahneh and Scoglio (2012) proposed an optimal information dissemination strategy to control the epidemic, in which

the susceptible group may receive an alert before being infected. The optimal control task is to construct the alert network, such that the susceptible persons are always warned in time, thus reducing the R_0 value; 3.) The work in Wan et al. (2008) proposed a spatially heterogeneous strategy for controlling the spread of the virus, where the population is categorized into different groups sharing the same or similar healing and infection rate.

After the outbreak of COVID-19, existing epidemic modeling and control techniques have been quickly adapted to capture particular characteristics of this virus. A quite detailed review to these adaptations is given in Kantner and Koprucki (2020). The work in Giordano et al. (2020) extended the SIS model to a more explicit one, the socalled SIDARTHE model accounting for the pandemic in Italy, which includes more disease-related status of the population at the beginning of COVID-19. Based on the SIDARTHE model, the work in Kantner and Koprucki (2020) proposed an optimal non-pharmaceutical intervention strategy for the case that a vaccine is never found. For the work by Köhler et al. (2020), which also considers the pandemic in Germany, the social distancing requirements are optimized through an MPC strategy in order to minimize the fatalities over a fixed period of time. The above work has all been written in the mid of the first wave of COVID-19, thus the main concern was limited to either finding a suitable model to reproduce the evolution of the pandemic during the first outbreak, or to evaluate whether the virus can be erased through a given policy. After the first wave, however, a fast elimination of the virus without vaccine has proven to be impossible in most countries (whereas the work by Liu and Stursberg (2021) has started to consider an optimized distribution of limited amount of available vaccines). The focus thus should be shifted to the question of how to properly utilize the experience gathered during the first wave, such that better intervention policies can be developed to mitigate the pandemic, until a vaccine is distributed to significant extent.

3. MODEL PREDICTIVE-BASED INTERVENTION POLICY MAKING

As the geographic position of a country plays an important role in analyzing the spread of diseases, a connection graph is constructed to model the adjacency to other countries, as well as the adjacency among different regions within a country. For one country to be investigated, let an overall set of nodes $N = \{1, \dots, n\} = N_s \cup N_f$ be given, where the nodes in N_s represent the regions of the country, while the nodes in N_f represent the neighboring countries. A directed graph $G = \{N, E\}$ is constructed, where E models the set of edges connecting the nodes. For the connection of any two local regions $i, j \in N_s$, two edges $\{e_{i,j},e_{j,i}\}\subset E$ are introduced (direction irrelevant). In case a region $i \in N_s$ shares border with a different country $j \in N_f$, a directed edge $e_{i,j} \in E$ (from j to i) is assigned. It is emphasized that the intervention policy to be addressed will take into account the pandemic in both local regions and neighboring countries, but only the control in the local regions is deployed. An adjacency matrix A can be determined for the graph, in which $\alpha_{ij} = 1$ if the edge $e_{i,j}$ exists and $\alpha_{ii} = 1$ for all $i \in N_s$, see Fig. 1.

In addition to the standard SIS model in (1), the Susceptible-Infected-Recovered (SIR) model, or the more complicated SIDARTHE model have been suggested to model and study the epidemic. The use of the SIR model is suitable if the recovered sub-population has significantly changed the population structure, and if this sub-population is constantly immune to reinfection. For COVID-19, however, the recovered sub-population still represents a relatively small share in many countries as of mid November 2020 and the risk of a reinfection can also not be excluded. The SIDARTHE model can cover more disease-related states and is suitable to model the epidemic in the first outbreak. For the period after the first wave, however, some states such as Diagnosed, Recognized or Threatened, may be no more crucial for long term policy making. The true critical factors after the first wave have actually been reduced to the daily number of active cases and death cases.

Note that the $p_i(t)$ in (1) represents the percentage of infected persons in the region i, i.e., as the number of population can be regarded as constant within the considered duration, and $p_i(t)$ changes with the number of active cases in region i. For the daily number of death cases (the mortality rate f), it has been observed that it grows rapidly if the number of critically infected patients exceeds the available intensive care units. By assuming that the number of critically infected patients also scales with the number of active cases, an active-case-based mortality curve is plotted in Fig. 2. Based on the relation in Fig. 2, the goal of minimizing the death cases in region i can be cast into a constraint $p_i(t) \leq p_i^c$, and a minimization of $p_i(t)$ in the latter problem.

Now, as both active and death cases in region i are related to $p_i(t)$, the SIS model in (1) is reformulated into the following form for each region $i \in N_s$:

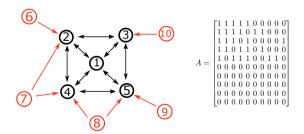


Fig. 1. Nodes in black represent local regions in the considered country, whereas nodes in red are neighboring countries (and the adjacency matrix on the right).

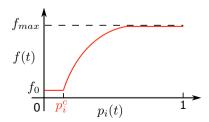


Fig. 2. Relation between f(t) and $p_i(t)$ in region i, where a threshold value p_i^c exists according to Kantner and Koprucki (2020).

$$\dot{p}_{i}(t) = (1 - p_{i}(t))\beta_{i}(\sum_{j \in N_{s}} \alpha_{ij}p_{j}(t) + \sum_{j \in N_{f}} \alpha_{ij}p_{j}(t)) - \delta_{i}p_{i}(t)$$
(3)

Compared to (1), the effect from other nodes to the local node i is divided into the one from the neighboring regions and the one from the neighboring countries. This is because only the $p_i(t)$ of local regions $i \in N_s$ are assumed to be controllable by the policies, while the $p_j(t)$, $j \in N_f$, of neighboring countries are obtained from prediction.

In this paper, the following inputs (or policies) and their impact are assumed to be at the disposal of the authorities: 1.) For each edge $e_{i,j}$ of the graph G, the entry $\alpha_{ij} \in \mathbb{R}^{\geq 0}$ in the adjacency matrix A can be selected from α_{min} to 1, where $\alpha_{ij}=1$ implies that no restriction is imposed on the connection, while α_{min} implies the most strict limitation. 2.) The requirement to wear masks or social distancing in region i will reduce the infection rate $\beta_i \in [\beta_{min}, \beta_{max}], \beta_i \in \mathbb{R}^{\geq 0}$. 3.) The hospital staff allocated for COVID-19 patients in region i will increase the healing rate $\delta_i \in [\delta_{min}, \delta_{max}], \delta_i \in \mathbb{R}^{\geq 0}$.

It is assumed that the mapping from different policies to the $\alpha_{ij},\ \beta_i,$ and δ_i values can be estimated according to the experiences from the first outbreak. These policies, however, will also lead to socio-economic costs. For a given planning horizon $[t_0,t_0+H]$, the policy is assumed to be adjusted every T days (thus changed for totally $H_c=\frac{H}{T}$ times within this horizon and being constantly for T days). Then the following socio-economic costs are considered: 1.) Decreasing the $\alpha_{ij}(k)$ in step $k\in\{0,\cdots,H_c-1\}$, implies a reduction of the interaction between different countries and regions, leading to a cost of:

$$J_{i,j}(\alpha_{ij}) := \sum_{k \in \{0, \dots, H_c - 1\}} c_{i,j} \cdot \alpha_{ij}(k), c_{i,j} < 0.$$
 (4)

2.) Decreasing the infection rate β_i leads to a higher load for local people, which is formulated by:

$$J_i(\beta_i) := \sum_{k \in \{0, \dots, H_c - 1\}} c_{b,i} \cdot \beta_i(k), c_{b,i} < 0.$$
 (5)

3.) Increasing the healing rate δ_i implies that more hospital staff is reserved for COVID-19 patients, thus the patients due to other diseases cannot be properly handled, i.e.:

$$J_i(\delta_i) := \sum_{k \in \{0, \dots, H_c - 1\}} c_{d,i} \cdot \delta_i(k), c_{d,i} > 0.$$
 (6)

The cost function terms in (4) – (6) are chosen to be linear in order to directly reflect the effect of the corresponding policy. In addition, as a frequent change of the policy should be avoided, the following cost function term is introduced to penalize large changes of the policy:

$$J_{cont,i} := \sum_{k \in \{0, \dots, H_c - 2\}} (\sum_{j \in N} (\alpha_{ij}(k+1) - \alpha_{ij}(k))^2$$

+
$$(\beta_i(k+1) - \beta_i(k))^2 + (\delta_i(k+1) - \delta_i(k))^2$$
. (7)

The overall cost function of i thus takes the form of:

$$J_{all,i} := \sum_{j \in N} J_{i,j}(\alpha_{ij}) + J_i(\beta_i) + J_i(\delta_i) + \int_{t_0}^{t_0+H} p_i(t) dt,$$

where the last term records the active cases over the considered horizon (each term of $J_{all,i}$ can also be weighted differently). The constraints on policy decisions consist of input constraints for α_{ij} , β_i and δ_i , and the state

constraint $p_i(t) \leq p_i^c$, i.e., the mortality threshold must not be exceeded. Finally, for decision time t_0 and for a given $p_i(t_0)$ in each local region $i \in N_s$, as well as a prediction $\hat{p}_j(t)$, $t \in [t_0, t_0 + H]$, on how the virus will spread in neighboring countries $j \in N_f$, the following MPC problem is solved to find the optimal intervention policy:

Problem 1.

$$\min_{\alpha_{ij}, \beta_i, \delta_i, \forall i \in N_s} \sum_{i \in N_s} J_{all,i} \tag{8}$$

s.t.: for all $i \in N_s, t \in [t_0, t_0 + H]$:

dynamics (3) with given prediction
$$\hat{p}_i(t)$$
, (9)

$$p_i(t) < p_i^c; \tag{10}$$

for all $k \in \{0, \dots, H_c - 1\}$:

$$\alpha_{ij}(k) \in [\alpha_{min}, 1], \forall j \in N$$
 (11)

$$\beta_i(k) \in [\beta_{min}, \beta_{max}], \ \delta_i(k) \in [\delta_{min}, \delta_{max}].$$
 (12)

Note that the threshold p_i^c here should not be exceeded in any time t, instead of only in decision time $t_{k\cdot T}$ (leading to a continuous-time optimization problem). The solution can be carried out, e.g. by using the multiple-shooting methods in Bock et al. (2000). Note that a high accuracy of the solution is desired as it refers to social costs and life of patients, while the solution time is not critical for H being chosen to several weeks. By using the receding-horizon scheme of MPC, the optimized policy of step k is applied, and the optimization is repeated after T days in the next step.

4. SIMULATION

To demonstrate which solutions are obtained from the considered MPC strategy, the selected scenarios are presented: Consider the connection graph in Fig. 1, and the percentages of infection $p_j(t), j \in N_f$, for all neighboring countries for totally 450 days as in Fig. 3. For the investigated country with five regions as in Fig. 1, the weight $\alpha_{ij}, i \neq j$, can take values in the interval [0.2, 1], and the infection rate β_i varies within $[5.4 \cdot 10^{-3}, 9 \cdot 10^{-3}]$, while the healing rate δ_i is in [0.014, 0.017]. The infection rate β_i has a larger range than δ_i , since the latter value cannot be significantly changed without efficient medicine. Default values of these variables are $\alpha_{ij} = 1$, $\beta_i = 9 \cdot 10^{-3}$ and $\delta_i = 0.014$. The threshold value is chosen to $p^c = 0.0001$.

Now, if the bang-bang intervention scheme is introduced in the studied country, i.e., whenever $p_i(t) \geq p^c$ applies in region i, this region is locked down in the next decision time: thus the weight α_{ij} of each edge connecting region i and the infection rate β_i are reduced to the minimum, and the healing rate β_i is increased to the maximum. The lock-down status then lasts for T=30 days up to the next decision time. The outcome by deploying this policy is illustrated in Fig. 4 and the lock-down sequences in all five regions are plotted in Fig. 5. One can notice that the $p_i(t)$ are beyond the threshold p^c in all regions for almost all the time, despite the frequent lock-downs and large fluctuations of $p_i(t)$ in other countries.

Next, assume that the development of $p_j(t)$ in the neighboring countries can be exactly predicted, i.e., $\hat{p}_j(t) = p_j(t)$, for all $j \in N_f$, $t \in \mathbb{R}^{\geq 0}$ (In case a prediction error exists, one can use the method in Liu and Stursberg (2019) to handle uncertain prediction problems in MPC). In the

first test, the prediction horizon is selected to be H=30 days (only one decision step), and the term (7) of the cost function is not considered. Then, by solving Problem 1 in a receding-horizon scheme in each decision time, the development of $p_i(t)$ in Fig. 6 is obtained, as well as the corresponding β_i and δ_i sequences, see Fig. 7 and 8 (The sequences of α_{ij} are not shown due to space limitations). Compared to the bang-bang intervention scheme, an overshoot over the threshold p^c has been successfully avoided, but a frequent change of the intervention policy occurs, which is certainly undesired and also unrealistic.

Accordingly, if the prediction horizon is extended to H=90 days (three decision steps) in Problem 1, and the term (7) is considered in the cost function, the development of $p_i(t)$ in Fig. 9 is obtained. Compared to the last test, the threshold p^c is reached after 270 days, while it was 120 days in Fig. 6, i.e. the spread of the virus has been slowed down. For the corresponding α_{ij} , β_i and δ_i sequences plotted in Fig. 9 to Fig. 12, they also appear to be more smoothly changed than in the last test. In general, the above simulation results establish the following fact: If the

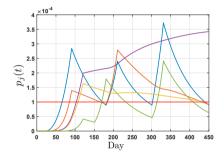


Fig. 3. Development of $p_i(t)$ in **neighboring** countries.

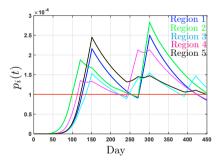


Fig. 4. Development of $p_i(t)$ in **local** regions using the bang-bang intervention scheme.

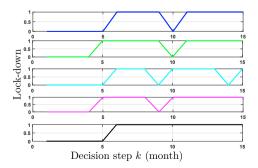


Fig. 5. Lock-down sequences by deploying the bang-bang scheme. The value 1 on vertical axis implies a lock-down is applied.

development of the pandemic can be well predicted based on the experiences from the first wave, and a sufficiently large horizon is taken into account when deciding upon the policy, a smooth strategy balancing the socio-economic costs and the risk of a new outbreak can be found, while the mortality rate is controlled to a relative low level.

5. CONSIDERATION OF UNCERTAINTIES

Note that the Problem 1 is a deterministic optimization problem without uncertainties. This setting, however, seems barely realistic if, e.g., intensive testing is not always possible. In particular, exact values of the infection rate β_i and healing rate δ_i , or the edge weight α_{ij} can hardly be determined in practice. More often, one can only identify possible ranges of these rates and weights. This challenges the MPC strategy which should be able to robustly satisfy the constraints in Problem 1. To this end, the min-max approaches tailored to robust MPC, see e.g. Campo and

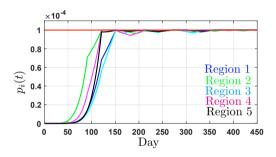


Fig. 6. Development of $p_i(t)$ in local regions by applying the MPC strategy with H = 30 days.

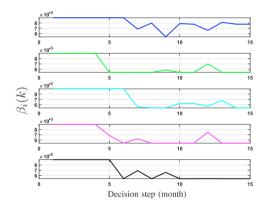


Fig. 7. Infection rate $\beta_i(k)$ when applying the MPC strategy with H = 30 days.

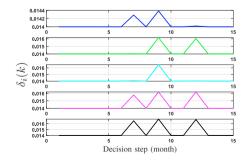


Fig. 8. Healing rate $\delta_i(k)$ when applying the MPC strategy with H=30 days.

Morari (1987), can be applied to satisfy the constraints even in the worst case. Another type of uncertainty often reported in media is a sudden outbreak in a hotspot of region i, which can be represented by a dramatical increase of $p_i(t)$ in short time. This hotspot scenario can be modeled by adding a bounded stochastic disturbance $\omega_i(t)$

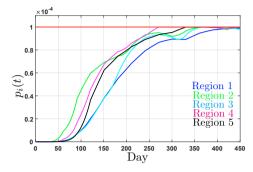


Fig. 9. Development of $p_i(t)$ when applying the MPC strategy with H = 90 days and the term (7).

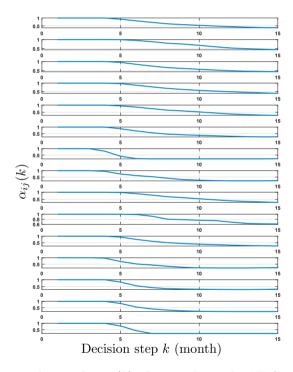


Fig. 10. The weight $\alpha_{ij}(k)$ when applying the MPC strategy with H = 90 days.

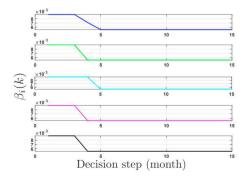


Fig. 11. Infection rate $\beta_i(k)$ when applying the MPC strategy with H = 90 days.

to the local dynamics (3), which follows a distribution that can be estimated from evolutions in the first year of the outbreak. Now, by replacing the dynamics (3) in Problem 1 by the stochastic model, one can either further apply the min-max approaches to ensure the robust satisfaction of the constraints. or adopt e.g. the technique of scenariobased MPC, see Bernardini and Bemporad (2009), to ensure that the constraints are satisfied in a mean-square sense. Furthermore, one can use the stochastic model to represent insufficient measurements of infected cases due to a lack of testing. In addition, it should be mentioned that Problem 1 only considers typical epidemic-related social-costs and constraints, while additional types are conceivable. For example, the economic costs such as the damage caused by lock-down, or constraints like available hospital staff can be included. Depending on the measurable data, Problem 1 should thus be adapted in every decision step k by identifying new instances of dynamics, costs, and constraints.

6. CONCLUSIONS

The objective of this paper was to illustrate that MPC strategies can make a meaningful contribution to determine intervention policies for a country against pandemics, and thus may serve as a tool for authorities. The background of the problem is that simple bang-bang schemes are not guaranteed to avoid a second wave of the pandemic, as shown by simulation and recent experiences. In addition, a frequent change of policies will also lead to negative effects on life and economy, and thus decreases the effectiveness. This paper has outlined how to determine ,, smoother" strategies by using MPC, taking the geographic position, the mortality rate, and the socio-economic costs into account. Simulation results have confirmed significant advantages compared to bangbang schemes. Upcoming work will take prediction and modeling uncertainties into account, in order to enhance robustness of the obtained policies.

REFERENCES

Bernardini, D. and Bemporad, A. (2009). Scenario-based model predictive control of stochastic constrained linear systems. In 48h IEEE Conf. on Decision and Control, 6333–6338.

Bock, H., Diehl, M., Leineweber, D., and Schlöder, J. (2000). A direct multiple shooting method for real-time

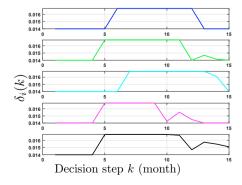


Fig. 12. Healing rate $\delta_i(k)$ when applying the MPC strategy with H=90 days.

optimization of nonlinear DAE processes. In *Nonlinear Model Predictive Control*, 245–267. Springer.

Campo, P. and Morari, M. (1987). Robust model predictive control. In *IEEE American Control Conf.*, 1021–1026.

Fall, A., Iggidr, A., Sallet, G., and Tewa, J. (2007). Epidemiological models and lyapunov functions. *Mathematical Modelling of Natural Phenomena*, 2(1), 62–83.

Giordano, G., Blanchini, F., Bruno, R., Colaneri, P., Di Filippo, A., Di Matteo, A., and Colaneri, M. (2020). Modelling the Covid-19 epidemic and implementation of population-wide interventions in Italy. *Nature Medicine*, 1–6.

Gourdin, E., Omic, J., and Van Mieghem, P. (2011). Optimization of network protection against virus spread. In 8th IEEE Int. Workshop on the Design of Reliable Communication Networks, 86–93.

Kantner, M. and Koprucki, T. (2020). Beyond just flattening the curve: Optimal control of epidemics with purely non-pharmaceutical interventions. *Journal of Mathematics in Industry*, 10(1), 1–23.

Kermack, W. and McKendrick, A. (1932). Contributions to the mathematical theory of epidemics. II.the problem of endemicity. *Proc. of the Royal Society of London. Series A*, 138(834), 55–83.

Khanafer, A., Başar, T., and Gharesifard, B. (2016). Stability of epidemic models over directed graphs: A positive systems approach. *Automatica*, 74, 126–134.

Köhler, J., Schwenkel, L., Koch, A., Berberich, J., Pauli, P., and Allgöwer, F. (2020). Robust and optimal predictive control of the Covid-19 outbreak. Annual Reviews in Control.

Liu, Z. and Stursberg, O. (2019). Recursive feasibility and stability of MPC with time-varying and uncertain state constraints. In 18th IEEE European Control Conf., 1766–1771.

Liu, Z. and Stursberg, O. (2021). A study on model-based optimization of vaccination strategies against epidemic virus spread. In 18th Int. Conf. on Informatics in Control, Automation and Robotics. - to appear .

Preciado, V., Zargham, M., Enyioha, C., Jadbabaie, A., and Pappas, G. (2013). Optimal vaccine allocation to control epidemic outbreaks in arbitrary networks. In 52nd IEEE Conf. on decision and control, 7486–7491.

Sahneh, F. and Scoglio, C. (2012). Optimal information dissemination in epidemic networks. In 51st IEEE Conf. on Decision and Control, 1657–1662.

Van Mieghem, P., Omic, J., and Kooij, R. (2008). Virus spread in networks. *IEEE/ACM Transactions On Networking*, 17(1), 1–14.

Wan, Y., Roy, S., and Saberi, A. (2007). Network design problems for controlling virus spread. In 46th IEEE Conf. on Decision and Control, 3925–3932.

Wan, Y., Roy, S., and Saberi, A. (2008). Designing spatially heterogeneous strategies for control of virus spread. *IET Systems Biology*, 2(4), 184–201.

Wang, Y., Chakrabarti, D., Wang, C., and Faloutsos, C. (2003). Epidemic spreading in real networks: An eigenvalue viewpoint. In 22nd IEEE Int. Symposium on Reliable Distributed Systems., 25–34.